

Mechanocardiographic assessment of left ventricular function in coronary artery disease*

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SUMMARY Multiple regression analysis was used in order to evaluate the independent contribution and combined use of mechanocardiographic indices for assessing cardiac function in 23 patients with coronary artery disease.

Three indices were derived from the quantitative displacement left apex cardiogram: the time from the onset of electrical depolarisation to the peak of the first derivative ($t_{\text{peak dD/dt}}$) and the first derivative normalised for the amplitude of the displacement ($dD/dt/D$) using for D total and developed displacement. From the external carotid pulse the ratio pre-ejection period to the ejection time (PEP/LVET) was calculated. Several invasive isovolumic and ejection phase indices of left ventricular function were calculated and used as dependent variables in the multiple regression analysis. The non-invasive indices were used as dependent variables. The index $dD/dt/D$ of the left apex cardiogram was significantly partially correlated with all invasive indices and demonstrated the highest t values. For PEP/LVET the t values were smaller and not always significant. No significant partial correlation was found for ($t_{\text{peak dD/dt}}$). The combined use of PEP/LVET and $dD/dt/D$ resulted in a better differentiation between normal and abnormal left ventricular function.

It is concluded that quantitative apex cardiography is superior to systolic time intervals for assessing left ventricular function in coronary artery disease though both methods offer independent information and should be considered complementary.

Systolic time intervals and indices derived from the left apex cardiogram have become established methods for the non-invasive evaluation of left ventricular function in man.¹⁻¹¹

There is no general agreement as to the value of these indirect methods for assessing myocardial function at rest in patients with coronary heart disease. Moreover, it is largely unknown to which degree each of these methods independently contributes to the assessment of left ventricular function. It may be postulated that the combined use of both non-invasive methods might result in a better evaluation of left ventricular performance.

In order to clarify this problem, comparisons were made with both angiographic and isovolumic indices of contractility in a group of patients with chronic

coronary artery disease. All indices, invasive and non-invasive, were obtained during the same catheterisation procedure and were correlated with each other by means of multiple linear regression analysis.

Methods

Twenty-three patients, two women and 21 men, with a mean age of 49 ± 11 (\pm SD) years were selected for the study. Chronic coronary artery disease, defined as stable angina pectoris, with or without previous myocardial infarction, was present in all patients. None of them had valvular lesions. All patients had regular sinus rhythm. Informed consent was obtained before the procedure.

TECHNIQUES

A selective coronary arteriography and a left

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ventriculogram in a 30 degree right anterior oblique position were performed in all patients. At least 15 minutes after the angiographic procedure a high-fidelity catheter tip micromanometer was introduced in the left ventricle (Telco or Millar Instruments).

Reference tracings were recorded through a side opening by means of an Elema EMT 456 strain gauge. The zero level was mid-thoracic.

The first derivative of left ventricular pressure (dP/dt) was obtained through resistance-capacitance differentiating circuits providing linear differentiation up to 45 Hz.

A calibrated displacement (D) left apex cardiogram was recorded by means of a piezoelectric crystal microphone (Elema-Schönander) with a time constant of four seconds. A description of the apparatus and the calibration procedure has been reported previously.^{8, 11}

The right external carotid pulse tracing was recorded by the same transducer.

Lead II of the electrocardiogram and the internal phonocardiogram, obtained by appropriate high-pass filtering from the micromanometer, were recorded simultaneously. The internal phonocardiogram was used for the determination of the onset of the high-frequency vibrations of the aortic component of the second heart sound (A2). Recordings were made on an eight-channel ink-jet recorder (Elema 81) at a paper speed of 250 mm/s. Before and after each experiment the simultaneity of the channels of the recorder was controlled.

CALCULATIONS

The following invasive indices were derived from the left ventricular pressure (LVP):

- the peak value of the first derivative of LVP: peak dP/dt (mmHg/s),
- maximum value of the ratio of the first derivative of LVP to the corresponding total pressure (P_t): $(dP/dt/P_t)_{\max}$ also called V_{pm} ,
- the linear extrapolation of this ratio to zero pressure called $V_{\max P_t}$,
- the ratio of the first derivative of LVP to the corresponding developed pressure (P_d = the instantaneous left ventricular pressure minus left ventricular end-diastolic pressure): $dP/dt/P_d$. The value of $dP/dt/P_d$ at the time of peak dP/dt represented (peak dP/dt)/ P_d ,
- the polynomial extrapolation of $dP/dt/P_d$ to zero pressure using P_d values > 10 mmHg was called $V_{\max P_d}$. As the c and k constants of the series elasticity were ignored, these indices were expressed per second.

From the left ventriculogram the following indices of myocardial function were calculated using the area-length method¹²:

- the ejection fraction (EF): the ratio of stroke volume to end-diastolic volume. In our laboratory the lower limit of normal (mean normal value minus 2 SD) for the EF was 0.64,
- the mean velocity of circumferential fibre shortening according to the method of Karliner *et al.*¹³ This index is expressed in circumferences per second (circ/s).

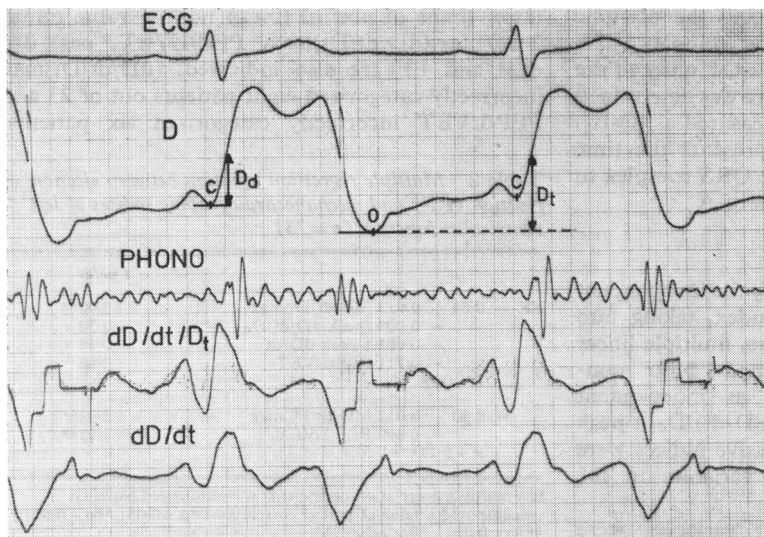


Fig. 1 Calculation of indices of left ventricular function from the quantitative displacement left apex cardiogram (QLAC). D, apical displacement; dD/dt , first derivative of QLAC; $dD/dt/D_t$, normalised first derivative of QLAC using total displacement (D_t); D_d , developed displacement; C, onset of systolic rise; O, protodiastolic nadir; ECG, electrocardiogram; PHONO, phonocardiogram.

Table 1 Indices of left ventricular function (mean \pm SD)

Invasive indices	Mean	\pm SD	Non-invasive indices	Mean	\pm SD
Peak dP/dt (mmHg)	1466.00	567.00	t-peak dD/dt (msec)	56.83	14.96
(dP/dt/P _i)max (s ⁻¹)	32.01	13.06	(dD/dt/D _i)max (s ⁻¹)	30.05	9.85
(peak dP/dt)/P _a (s ⁻¹)	29.49	10.31	(peak dD/dt)/D _a (s ⁻¹)	32.22	9.14
Vmax P _i (s ⁻¹)	42.09	14.88	PEP/LVET	0.497	0.132
Vmax P _a (s ⁻¹)	78.27	26.05			
EF	0.511	0.207			
Mean Vcf (circ/s)	1.028	0.691			

For abbreviations of different indices see text.

The quantitative left apex cardiogram provided the non-invasive indices listed below:

- the time from the onset of electrical depolarisation to the peak value of the first derivative (t peak dD/dt), expressed in milliseconds (ms),
- the normalised first derivative of the left apex cardiogram (dD/dt/D) using for D both total (D_i) and developed (D_a) displacement. D_i is measured with the 0 point (protodiastolic nadir) and D_a with the C point (onset of systolic contraction) of the apex cardiogram as reference zero point (Fig. 1). dD/dt/D_i is calculated electronically by means of a logarithmic amplifier and differentiator and the maximum value is termed (dD/dt/D_i)max. dD/dt/D_a is measured manually and its value at the time of peak dD/dt is called (peak dD/dt)/D_a. Both indices are expressed per second.

From the right external carotid pulse tracing the ratio pre-ejection period to left ventricular ejection time, PEP/LVET, was calculated. The beginning of the upstroke of the carotid pulse was determined by extending the systolic rising and the diastolic descending limb of the preceding complex. The intersection was considered as the exact onset of the upstroke.¹⁴ The nadir of the incisura was determined by simple inspection. PEP was measured as (Q-A₂) minus LVET, where (Q-A₂) represents the time interval from the beginning of the QRS complex to the first high-frequency vibrations of A₂.

STATISTICAL CALCULATIONS

In order to evaluate and to quantify the independent contribution of a non-invasive index, taking into account the interaction with others, multiple linear regression analysis was performed. Four non-invasive parameters were used as independent variables: (dD/dt/D_i)max, (peak dD/dt)/D_a, t peak dD/dt, and PEP/LVET. All invasive indices were successfully used as dependent variables in the regression model.

The insignificant independent variables were

deleted stepwise until only significant variables remained.

Results

The mean values (\pm SD) of all invasive and non-invasive indices are listed in Table 1. A normal left ventricular function (EF \geq 0.64 and absence of segmental contraction abnormalities) was found in seven patients.

In the multiple regression analysis the same four non-invasive indices are used as independent variables. All the invasive indices are successively used as dependent variables.

Multiple regression analysis with ejection fraction as dependent variable reveals a significant t value for (dD/dt/D_i)max and PEP/LVET. The apex cardiographic index presents the highest t value (Table 2). With peak dP/dt of the left ventricular pressure similar results are obtained (Table 3). The individual values and the single linear correlations of these indices are shown in Fig. 2 and 3. The lower limits of normal (mean normal value minus 2 SD) for (dD/dt/D_i)max,⁸ PEP/LVET,³ peak dP/dt,¹⁵ and EF are also indicated. (dD/dt/D_i)max incorrectly categorised eight patients out of 23 and PEP/LVET incorrectly categorised six patients.

Table 2 Multiple regression equation between ejection fraction (EF) and mechanocardiographic indices of left ventricular function (n=23)

	t value
EF = 0.64 + 0.013 (dD/dt/D _i)max	+3.02**
- 0.003 (peak dD/dt)/D _a	-0.50
- 0.001 t-peak dD/dt	-0.44
- 0.711 PEP/LVET	-2.66*
R=0.78	
EF = 0.50 + 0.012 (dD/dt/D _i)max	+3.92***
- 0.699 PEP/LVET	-3.12**
R=0.77***	

R=multiple correlation coefficient; n=number of patients;
t=computed t value of partial correlation; *p<0.05; **p<0.01;
***p<0.001. For other abbreviations see text.

However, an abnormality in one or two of these measurements was associated with an abnormal ejection fraction in 22 out of the 23 patients. In 11 out of 23 patients at least one non-invasive index and in nine patients both indices correctly differentiate between normal and abnormal values of peak dP/dt (Fig. 3). There is no significant linear correlation between PEP/LVET and $(dD/dt/D_i)_{\max}$ ($r = -0.16$ NS).

Using mean Vcf as dependent variable an independent significant contribution is found only for $(dD/dt/D_i)_{\max}$ (Table 4). The same holds for the multiple correlation with Vpm (Table 5).

Table 6 summarises all the significant partial correlations found in the multiple regression analysis. Whether an injection phase index or an isovolumic pressure index is used as dependent variable, the normalised first derivative of the left apex cardiogram is always significantly correlated with the index under consideration and demonstrates the highest t values. The ratio PEP/LVET presents a significant partial correlation only with EF, peak dP/dt , and $(\text{peak } dP/dt)/P_a$. No significant partial correlation can be demonstrated for the index t peak dD/dt .

Discussion

Assessment of cardiac dynamics and myocardial function using external pulse tracings remains an important goal in non-invasive diagnostic cardiology. Among these the external carotid pulse and the left apex cardiogram are certainly the most commonly used. The apex cardiogram has been used as a substitute for pressure in timing left ventricular events,^{1 18-18} and constructing pressure dimension loops.¹⁷ When the delay for pulse wave

Table 4 Multiple regression equation between mean velocity of circumferential fibre shortening (mean Vcf) of left ventricle and mechanocardiographic indices of left ventricular function ($n=23$)

	<i>t</i> value
Mean Vcf = $1.27 + 0.051 (dD/dt/D_i)_{\max}$	$+2.93^{**}$
- $0.022 (\text{peak } dD/dt)/D_a$	-0.90
- $0.007 t\text{-peak } dD/dt$	-0.54
- 1.400 PEP/LVET	-1.32
R=0.67	
= $0.80 + 0.046 (dD/dt/D_i)_{\max}$	$+3.14^{**}$
- $0.013 (\text{peak } dD/dt)/D_a$	-0.73
- 1.503 PEP/LVET	-1.47
R=0.66	
= $0.39 + 0.044 (dD/dt/D_i)_{\max}$	$+3.34^{**}$
- 0.001 PEP/LVET	-1.29
R=0.65	
= $-0.26 + 0.043 (dD/dt/D_i)_{\max}$	$+3.55^{**}$
$r=0.61^{**}$	

For abbreviations see Table 2.

transmission is taken into account, the external carotid pulse closely resembles the aortic pressure.^{6 14}

Morphological changes of these tracings already offer many diagnostic possibilities as to valvular lesions and cardiac performance. Both tracings also provide a quantitative estimate of left ventricular function. Both methods, however, also have their limitations: for the left apex cardiogram, the absence of a true zero level and a still incomplete understanding of the determinants of its time course and morphology; for systolic time intervals, the change in opposite direction of some determinants of these intervals during changes in the inotropic state of the heart.¹⁹

The time interval from the onset of electrical depolarisation to the peak of the first derivative of the left apex cardiogram has been proposed as a quantitative index in assessing left ventricular function on the apex cardiogram.^{2 20} Subsequently the concept of 'amplitude normalisation' was introduced. It was found that the left ventricular pressure plays a predominant role in shaping the morphology of the left apex cardiogram²¹ and that a distinct similarity in slope exists between the left apex cardiogram and the left ventricular pressure during isovolumic contraction.⁷ In view of these findings the left apex cardiogram was calibrated and its first derivative was normalised for the amplitude of the apical impulse. Recent studies from our laboratory demonstrated the clinical value and advantages of the calibrated apex cardiogram and its normalised first derivative.^{8 11}

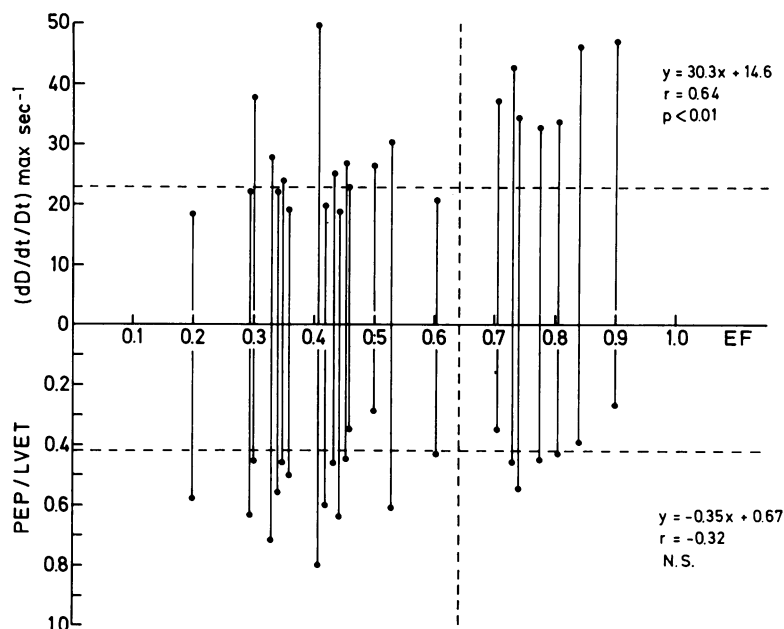
Several authors have correlated systolic time intervals with other measurements of cardiac performances.^{3 4 6 9} The index PEP/LVET is used

Table 3 Multiple regression equation between peak value of first derivative of left ventricular pressure (peak dP/dt) and mechanocardiographic indices of left ventricular function ($n=23$)

	<i>t</i> value
Peak dP/dt = $687.0 + 21.7 (dD/dt/D_i)_{\max}$	$+1.94$
+ $22.7 (\text{peak } dD/dt)/D_a$	$+1.46$
- $1.7 t\text{-peak } dD/dt$	-0.21
- 1445.2 PEP/LVET	-2.14^*
R=0.82	
= $805.0 + 22.9 (dD/dt/D_i)_{\max}$	$+2.45^*$
+ $20.5 (\text{peak } dD/dt)/D_a$	$+1.83$
- 1419.4 PEP/LVET	-2.19^*
R=0.82	
= $1444.1 + 32.5 (dD/dt/D_i)_{\max}$	$+3.97^{***}$
- 1958.2 PEP/LVET	-3.22^{**}
R=0.78^{***}	

For abbreviations see Table 2.

Fig. 2 Individual values and single linear correlations of ejection fraction (EF), ratio pre-ejection period/ejection time (PEP/LVET), and normalised first derivative of apex cardiogram ($dD/dt/D_t$) max. Dotted lines indicate lower limits of normal.



and Garrard *et al.*⁴ have shown the highest correlation coefficient with the angiographic ejection fraction ($r = -0.90$). In the latter study various forms of heart disease were included, with extreme values for ejection fraction (ranging from 0.08 to 0.84). When, however, it was applied to patients with coronary artery disease the correlation coefficients were smaller.^{9 22 23}

At present there is no single undisputed invasive

index for assessing myocardial contractility in man. Both isovolumic and ejection phase indices of contractility are susceptible to criticism and have their advantages and limitations.^{24 25} In order to evaluate the usefulness and the relative importance of calibrated apex cardiography and systolic time intervals for assessing left ventricular function in coronary artery disease, comparisons were made with both invasive methods. Multiple linear

Fig. 3 Individual values and single linear correlations of peak value of first derivative left ventricular pressure (peak dP/dt), ratio pre-ejection period/ejection time (PEP/LVET), and normalised first derivative of apex cardiogram ($dD/dt/D_t$) max. Dotted lines indicate lower limits of normal.

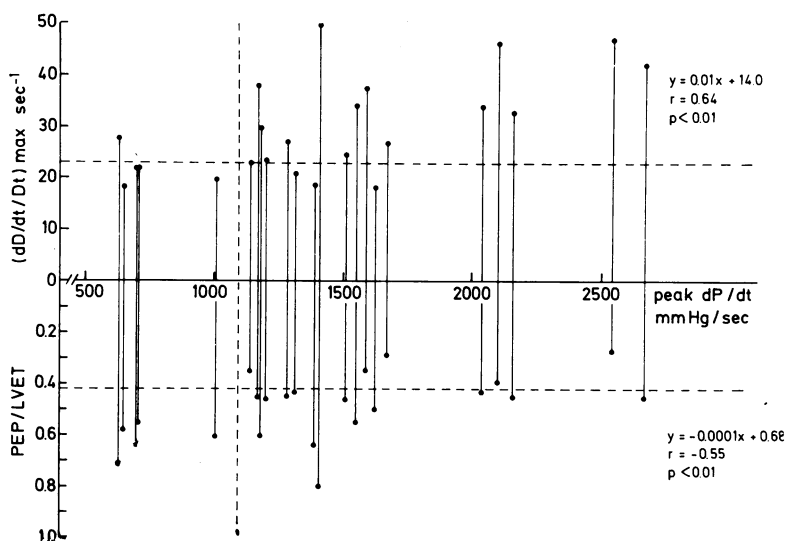


Table 5 Multiple regression equation between peak measured velocity of shortening of contractile elements (Vpm) and mechanocardiographic indices of left ventricular function (n=23)

		<i>t</i> value
Vpm =	37.74 + 1.20 (dD/dt/D _i)max	+4.21***
	- 0.60 (peak dD/dt)/D _a	-1.50
	- 0.18 t-peak dD/dt	-0.90
	- 24.75 PEP/LVET	-1.43
	R=0.77	

=	25.03 + 1.07 (dD/dt/D _i)max	+4.38***
	- 0.36 (peak dD/dt)/D _a	-1.22
	- 27.53 PEP/LVET	-1.63
	R=0.76	

=	13.88 + 0.90 (dD/dt/D _i)max	+4.42***
	- 18.13 PEP/LVET	-1.19
	R=0.73	

=	3.67 + 0.94 (dD/dt/D _i)max	+4.63***
	r=0.71	

For abbreviations see Table 2.

regression analysis was used to quantify the individual independent contribution of each non-invasive index.

From the statistical results it is clear that most important indirect information on left ventricular function is provided by the normalised derivative of the apex cardiogram. This is true whether angiographic or pressure indices of cardiac per-

equation with the EF and peak dP/dt of the left ventricular pressure. It should be noted that the present investigations were limited to resting frequencies. Though better identification of abnormal cardiac function in coronary artery disease during exercise is reported using systolic time intervals,^{22, 27} the overall correlations with invasively determined indices of cardiac performance have improved only a little.²²

It is noteworthy that in this group of patients and with this regression model, no significant independent information on left ventricular function is provided by the index t peak dD/dt. The most logical explanation appears to be that the pre-ejection period and the normalised first derivative of the left apex cardiogram already contain most of the information provided by this index.

From our data it can be concluded that quantitative apex cardiography is a useful non-invasive tool for the evaluation of cardiac function in patients with coronary artery disease. In the group of patients studied, it is superior to systolic time intervals.

Although each method alone is not a strong indication of the state of the left ventricle in chronic coronary artery disease, both methods contain useful independent information and should be used together.

Table 6 Multiple regression analysis between invasive and non-invasive indices of left ventricular function in patients with chronic coronary artery disease (n=23)

Dependent variables	Independent variables				Correlation coefficient (R, r)
	(dD/dt/D _i)max	(peak dD/dt)/D _a	t peak dD/dt	PEP/LVET	
EF	***			**	0.77***
Mean Vcf	**				0.61**
(dP/dt/P _i) max or Vpm	***				0.71***
Vmax P _i	**				0.62**
peak dP/dt	***			**	0.78***
(peak dP/dt)/P _a		***		*	0.83***
Vmax P _a		**			0.57**

*p < 0.05; **p < 0.01; ***p < 0.001. For abbreviations of different indices see text.

formance are used as dependent variables. When developed pressure is used in the calculation of the isovolumic indices, the corresponding apex cardiographic indices based on developed displacement are involved, since the O-C amplitude of the left apex cardiogram reflects left ventricular end-diastolic pressure.¹⁶ Furthermore, the concept of normalisation of the first derivative, also termed 'normalised velocity', can be considered as a general index for assessing cardiac performance, equally applicable to invasive and non-invasive methods.^{11, 26}

The ratio PEP/LVET also provides independent significant information, as shown by the regression

References

- Tavel ME, Campbell RW, Feigenbaum H, Steinmetz EF. The apexcardiogram and its relationship to hemodynamic events within the left heart. *Br Heart J* 1964; **27**: 829-39.
- Reale A. Evaluation of the contractile state of the human heart from the first derivative of the apexcardiogram. *Circulation* 1967; **36**: 933-41.
- Weissler AM, Harris WS, Schoenfeld CD. Bedside technics for the valuation of ventricular function in man. *Am J Cardiol* 1969; **23**: 577-83.
- Garrard CJ Jr, Weissler AM, Dodge HT. The relationship of alterations in systolic time intervals to ejection

- fraction in patients with cardiac disease. *Circulation* 1970; **42**: 455-62.
- ⁵Sutton GC, Prewitt TA, Craige E. Relationship between quantitated precordial movement and left ventricular function. *Circulation* 1970; **41**: 179-90.
- ⁶Martin CE, Shaver JA, Thompson ME, Reddy PS, Leonard J. Direct correlation of external systolic time intervals with internal indices of left ventricular function in man. *Circulation* 1971; **44**: 419-31.
- ⁷Denef B, De Geest H, Kesteloot H. Influence of changes in myocardial contractility on the height and slope of the calibrated apex-cardiogram. *Am J Cardiol* 1973; **32**: 662-9.
- ⁸Denef B, Popeye R, De Geest H, Kesteloot H. On the clinical value of calibrated displacement apex-cardiography. *Circulation* 1975; **51**: 541-51.
- ⁹Lewis RP, Boudoulas H, Welch TG, Forester WF. Usefulness of systolic time intervals in coronary artery disease. *Am J Cardiol* 1976; **37**: 787-96.
- ¹⁰Manolas J, Wirz P, Rutishauser W. Relationship between duration of systolic upstroke of apexcardiogram and internal indexes of myocardial function in man. *Am Heart J* 1976; **91**: 726-34.
- ¹¹Van de Werf F, Piessens J, De Geest H, Kesteloot H. Normalized first derivative of the left apexcardiogram in the assessment of left ventricular function. *Am J Cardiol* 1976; **37**: 1059-64.
- ¹²Sandler H, Dodge HT. The use of single plane angiocardigrams for the calculation of left ventricular volume in man. *Am Heart J* 1968; **75**: 325-34.
- ¹³Karliner JS, Gault J R, Eckberg P, Mullins CB, Ross J Jr. Mean velocity of fiber shortening: a simplified measure of left ventricular contractility. *Circulation* 1971; **44**: 323-33.
- ¹⁴Van de Werf F, Piessens J, Kesteloot H, De Geest H. A comparison of systolic time intervals derived from the central aortic pressure and from the external carotid pulse tracing. *Circulation* 1975; **51**: 310-6.
- ¹⁵Quinones MA, Gaasch WH, Alexander JK. Influence of acute changes in preload, afterload, contractile state and heart rate on ejection and isovolumic indices of myocardial contractility in man. *Circulation* 1976; **53**: 293-302.
- ¹⁶Willems J. *The normal apexcardiogram*. Brussels: Arsacia, 1973: 215-60.
- ¹⁷Venco A, Gibson D, Brown D. Relation between apex cardiogram and changes in left ventricular pressure and dimension. *Br Heart J* 1977; **39**: 117-25.
- ¹⁸Van de Werf F, Piessens J, Kesteloot H, De Geest H. Value of apexcardiography for the timing of left ventricular events in man. *Acta Cardiol (Brux)* 1978; **33**: 295-303.
- ¹⁹Kesteloot H. On the clinical value of mechano-cardiography. *Eur J Cardiol* 1976; **4**: 393-6.
- ²⁰Vetter WR, Sullivan RW, Hyatt KH. Assessment of quantitative apexcardiography. A non-invasive index of left ventricular function. *Am J Cardiol* 1972; **29**: 667-71.
- ²¹Willems J, Kesteloot H, De Geest H. Influence of acute hemodynamic changes on the apexcardiogram in dogs. *Am J Cardiol* 1971; **29**: 504-13.
- ²²Gleichmann U, Neitzert A, Mertens HM, Schmidt H, Sigwart U, Steiner J. Correlation between left ventricular function at rest and during exercise and systolic time intervals in coronary heart disease (abstract). *Eur J Cardiol* 1976; **4**: 399.
- ²³Sohn YJ, Stack MR, Taylor ML, Weissler AM. Sensitivity and specificity of systolic time intervals in detecting abnormal left ventricular performance in coronary artery disease (abstract). *Circulation* 1977; **55** and **56**: Suppl. III, 210.
- ²⁴Ross J Jr, Peterson KL. On the assessment of cardiac inotropic state. *Circulation* 1973; **47**: 435-8.
- ²⁵Peterson KL, Skloven D, Ludbrook P, Uther JB, Ross J Jr. Comparison of isovolumic and ejection phase indices of myocardial performance in man. *Circulation* 1974; **49**: 1088-101.
- ²⁶Mirsky I, Pasternac A, Ellison RC. General index for the assessment of cardiac function. *Am J Cardiol* 1972; **30**: 483-91.
- ²⁷Van der Hoeven G, Clerens P, Donders J, Beneken J, Vonk J. A study of systolic time intervals during uninterrupted exercise. *Br Heart J* 1977; **39**: 242-54.

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